THE MAGNITUDE OF NOSOCOMIAL INFECTIONS AMONG INTENSIVE CARE UNIT PATIENTS AT MUHIMBILI MEDICAL CENTRE, DAR ES SALAAM, TANZANIA.

BY

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the University of Dar es Salaam a dissertation entitled: *The magnitude of Nosocomial Infections among Intensive Care Unit Patients at Muhimbili Medical Centre,* in partial fulfillment of the requirements for the degree of Master of Medicine (Anaesthesia).

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DECLARATION

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I, Mpoki Mwasumbi Ulisubisya, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

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DEDICATION

To Elena and Ulisubisya

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ABSTRACT

The determination of the prevalence of nosocomial infections, associated risk factors, and the antimicrobial susceptibility pattern of bacterial isolates among patients admitted to the intensive care unit was carried out.

Critically ill patients admitted to the intensive care unit, medical staff and equipment were evaluated, samples were taken for gram staining, culture and the determination of antimicrobial susceptibility pattern of bacterial isolates.

Of the two hundred and sixty two patients admitted during the study period, 200 were recruited into the study; they comprised of 179 (68.3%) males and 83 (31.7%) females. Head injured patients accounted for 15.5% of the total admissions, followed by tetanus (12.0%), post craniotomy, cerebral tumors, dental conditions, septicemia, ruptured viscera and burn patients made up the rest of the admitted patients. ICU equipment were found to harbor pathogenic organisms, medical staff working in the ICU were also found to harbor pathogenic which could infect patients in the ICU (p=0.007).

Pneumonia afflicted 62.5% of patients and the leading pathogen was *Klebsiella spp* (38.4%), ventilator associated pneumonia was seen in 57.6% of patients. Urinary tract infection was diagnosed in 90% of patients, and the leading pathogen isolated was *Klebsiella spp* (36.7%). *Pseudomonas aeruginosa* was isolated in 15.0% and 36.4% patients with bacteremia and surgical wound infections, respectively. Their antimicrobial susceptibility pattern were determined. Means for prevention and control of nosocomial infections are suggested.

Nosocomial infections are significantly prevalent in patients admitted to the Intensive care unit. Gram-negative organisms are the leading pathogens in these conditions. Equipment and medical staff in the Intensive Care unit harbor certain infectious micro-organisms which could infect patients admitted therein. In the absence of working surveillance system in place, nosocomial infections will continue to be a major factor in the increased morbidity and mortality for patients admitted. As bacteria resistance to antimicrobials is a potential problem in the ICU, means must be put in place to effect continuous surveillance of antimicrobial resistance.

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List of abbreviations:

1. AIDS	Acquired immunodeficiency syndrome
2. ARDS	Adult respiratory distress syndrome
3. B cells	B Lymphocytes
4. *C.difficile*	*Clostridium difficille*
5. *E.coli*	*Escherichia coli*
6. ETT	Endotrachea tube
7. HIV	Human Immunodeficiency virus
8. ICU	Intensive Care Unit
9. IL-1	Interleukin 1
10. *K.spp*	*Klebsiella.spp*
11. MMC	Muhimbili Medical Centre
12. MRSA	Methicillin Resistant *Staphylococcus aureus*
13. MSSA	Methicillin Sensitive *Staphylococcus aureus*

14. *M.tuberculosis*	*Mycobacterium tuberculosis*
15. N.b	No bacteria isolated
16. N.pro	Nasal prong
17. OPD	Out Patient Department
18. PMN	Polymorphonucleocytes
19. *P.aeruginosa*	*Pseudomonas aeruginosa*
20. *S.aureus*	*Staphylococcus aureus*
21. *S.epidemidis*	*Staphylococcus epidemidis*
22. S.cath	Suction catheter
23. T cells	T lymphocytes
24. UCI	Unidentified Coliform Isolated
25. UTI	Urinary tract infections
26. V.tube	Ventilator tubing

PART I

INTRODUCTION AND LITERATURE REVIEW

Nosocomial infection is a medical term that describes hospital-associated infections that arise during hospitalization as a complication of other illnesses[1]. The definition is based on several important principles.

First, information used to determine the presence and classification involves various combinations of clinical findings and results of laboratory and other diagnostic tests. Clinical evidence is derived from direct observation of the patient or review of information in the patient's chart or other ward or unit records. Laboratory evidence consists of results of cultures, antigen- or antibody–detection tests, and microscopic visualisation methods. For infections in which clinical manifestations are different in neonates and infants than in older persons, specific criteria are utilized.

Second, a physician's or surgeon's diagnosis of infection derived from direct observation during surgery 'endoscopic examination' or other diagnostic procedures, or based on clinical judgement, is an acceptable criterion for an infection, unless there is compelling evidence to the contrary (e.g. information written on the wrong

patient's record or a presumptive diagnosis that was not substantiated by subsequent studies).

Third, for an infection to be termed nosocomial, there must be no evidence that the infection was present or incubating at the time of hospital admission. An infection however that occurs in the following special situations is considered nosocomial (1) Infection that is acquired in the hospital and becomes evident after hospital discharge and (2) Infection of a newborn that is the result of passage through the birth canal.

Fourth, infection that occurs as a result of the following special situations is not considered nosocomial:

(1) Infection that is associated with a complication or extension of infection(s) already present on admission, unless a change in pathogen or symptoms strongly suggests the acquisition of a new infection

(2) Infection in an infant that is known or proved to have been acquired transplacentally and becomes evident shortly after birth.

Fifth, except for a few situations that are referred to in the definitions, no specific time during or after hospitalization, is given to determine

whether the infection is nosocomial or community-acquired. Thus each is assessed for evidence that links it to hospitalization[2].

Infections associated with hospitalisation can be either community acquired or hospital acquired (nosocomial). Community acquired infections are those present or incubating at the time of hospital admission, while those manifesting during hospitalization and within 14 days of hospital discharge are categorised as nosocomial.

Sources of nosocomial infections

It is important to recognise the peculiar infection hazards posed by the hospital; it is there that the most seriously infected and most susceptible patients are housed and often cared for by the same staff. The infectious agents responsible for nosocomial infections arise from various sources; these include personnel, the environment and medical equipment. Many infectious agents however are endogenous originating from the patient's own normal flora. It has been said that two thirds of respiratory infections are caused by pathogens colonising the oropharynx though others may be exogenous. The factors involved in the pathogenesis of such infections are essentially the same in or out of hospital. They include any debilitating disease, additional risks imposed by treatments that breach the normal

defence barriers, and the risk of infection is generally related to the extent of trauma and severity of underlying illness.

Hospital personnel

Physicians, nurses, students, therapists, and any others who come into contact with the patient may transmit infection, the mechanisms being usually by direct contact via the hands of the medical attendant. Many hospital outbreaks have been traced to hospital personnel, who continue to care for patients despite an overt infection. Transmission is usually by direct contact, although airborne transmission is also possible. A third source is the person who is not ill but carrying a virulent strain. *Staphylococcus aureus* (*S.aureus)* carriers are most frequently involved. Nasal carriage *S.aureus* is most important, but sites such as the perineum and axilla have also been responsible for outbreaks. The hospital air, walls, floors, linens are not sterile and thus could serve as a source of organisms causing nosocomial infections. However, with the exception of the immediate vicinity of a case or carrier, transmission through air or formites is much less important than that caused by personnel or equipment[3]. Exceptions are instances in which organisms are numerous and patients particularly susceptible or when a particular site is unusually vulnerable (heart valves in

valvular surgery[3] or prosthetics implants in bone surgery) due to a possible vegetation growth on the endocardium providing a convenient growth site for micro organisms.

Medical devices

Medical devices such as arterial lines, venous lines, endotracheal tubes, oxygen face masks, nasal prongs urethral catheters and others that support or monitor basic body functions, carry a risk of nosocomial infections. This is because they bypass normal defence barriers, providing micro-organisms access to normally sterile fluids and tissues.

The risk of infection is related to the degree of debilitation of the patient and various factors concerning the design and management of the device. Any device that crosses the skin or a mucosal barrier will allow flora in the patient or environment to gain access to deeper sites around the outside surface. Possible access inside the device (e.g. in the lumen) adds another risk. With some devices, such as urinary catheters, contamination is avoidable, in others, such as respirators, complete sterility is either impossible or impractical to achieve[3].

Types of nosocomial infections:

Urinary tract infections

Urinary tract infections (UTIs) are the most common hospital acquired infections, accounting for about 40 to 45 percent of all nosocomial infections and generally are the easiest to treat with the least severe sequelae[4]. Pneumonia accounts for 15 to 20 percent, and bacteremia, mainly associated with intravascular devices, 5 to 7 percent[4].

In a study that controlled for potential confounding factors such as severity of illness, length of hospitalization, and duration of catheterization, the overall case-fatality rate was 2.8 times higher in patients with bacteriuria than in patients without bacteriuria[5]. A follow-up study of sealed catheter junctions showed a decrease in UTIs[5].

Four principal risk factors have been associated repeatedly with the development of UTI in hospitalized patients: female sex, duration of urinary catheterization, absence of systemic antibiotics, and breach of appropriate catheter care. The pathogenesis of catheter-associated UTI appears to differ in men and women. In women, periurethral

colonisation with faecal flora, with tracking of organisms up the catheter to the bladder, resembles the pathogenesis of UTI in noncatheterized female patients, in whom bacteria track up the short female urethra. In contrast, periurethral colonisation often cannot be demonstrated in men, and the majority of infections seem to arise from intraluminal spread of organisms to the bladder. Some organisms (e.g. *Proteus spp and Pseudomonas spp*) seem to facilitate the growth of a biofilm along the inside of the urinary catheter which encrusts and obstructs the flow of urine.

While UTI is an extremely common nosocomial infection, it is important to define infection precisely. Especially in evaluating a febrile hospitalized patient, it is crucial to think carefully about all possible sources of infection and not assume UTI is the probable cause[5].

In patients with fever with no other symptoms or signs referable to the urinary tract, one should look for ancillary findings suggestive of urinary tract involvement, such as white blood cells without epithelial cells in the urine sediment or leukocyte esterase or nitrite on urinalysis. Inability to recover an organism or the same organism in repeat culture, particularly if the patient does not respond to antibiotics, should raise some questions about the validity of

diagnosis of UTI. Isolation of two or more bacteria from a single specimen is most likely due to contamination unless there is reason to suspect a bladder diverticulum or a perinephric abscess[5].

Fever

Several other types of infections may cause fever in the hospitalised patient, and these have to be considered in the differential diagnoses of new fever. In patients who have received antibiotics, even a single dose as surgical prophylaxis, antibiotic-associated diarrhoea may develop fever. This is usually caused by the spore-forming organisms *C.difficile*, which produces toxins that cause diarrhoea. Some patients may appear quite toxic with this infection, with high fevers, leukocytosis, and profuse diarrhoea. Hands of hospital personnel have been implicated as a mode of transmission of this organism, as have the electronic rectal thermometers despite use of individual covering sheaths for each patient. The colon may become colonised with *C.difficile* while the patient is in the hospital, diarrhoea may not present until after discharge. Other infections to consider in the hospitalized patient with fever include decubitus ulcers, and sinusitis, in patients with nasotracheal tubes[6].

Drugs are the major non-infectious cause of fever, drug fever may

occur with or without an accompanying rash. Particular agents associated with drug fever include phenytoin, H_2 blockers, procainamide. Antibiotics, most notably sulfonamides. Drug fever can be quite high in some patients and may take up to five days to resolve after removal of the offending agent.

Phlebitis, often occurring at the site of an old intravenous line and sometimes followed by suppurative thrombophlebitis with clots or septic emboli, and pulmonary emboli especially in patients on prolonged bed rest[6].

Respiratory tract infections

The Intensive Care Unit (ICU) is one of the most common locations in the hospital for the development of nosocomial respiratory tract infections. Most ICU patients require care with use of respiratory support equipment[3], such as endotracheal tubes, oxygen masks, and ventilators. Oropharyngeal and gastric colonization play a critical role in the pathogenesis of pneumonia in hospitalised patients. The signs of pneumonia are more subtle, and therefore, diagnosis of pneumonia is often more complex in ICU patients, especially those who are intubated.

Chest x-ray films are much more difficult to interpret, due to the presence of fluid overload, congestive heart failure, and adult respiratory distress syndrome (ARDS) are all common findings in intubated patients. Polymorphonuclear leukocytes (PMNs), are present on gram's stain of purulent secretions common in intubated patients. This means that a change in output or character of these secretions would be an important clue to pneumonia. Another subtle sign of pneumonia in the intubated patient is a requirement for change in ventilator settings in the absence of fluid overload, a mechanical alteration such as shift in endotracheal tube placement or the presence of pneumothorax.

Most patients dying in the ICU, have at least one episode of infection, pneumonia accounting for more deaths than infection at any other site[7]. With the HIV infection so rampant most immunocompromised and or AIDS patients are at an increased risk of acquiring tuberculous infection, and developing clinical disease if exposed to patients with open tuberculosis. Hence because of the HIV/AIDS epidemic, tuberculosis is likely to become an important and common nosocomial infection[8,9].

Immunocompromised host

Although immunosuppressed hosts are especially vulnerable to infections acquired in a hospital, there are common nosocomial infections that occur even in normal hosts. In the immunocompromised patients the defect determine the anticipated infection, which depends on whether the defect is secondary to chemotherapy, immunosuppression related to organ or bone marrow transplantation[10].

Neutropenic patients are unusually susceptible to bacterial infections, especially the common gram positive and gram-negative organisms found on the skin and in the bowel. While considering these, it is essential to note that cephalosporins can cause bone marrow suppression and vancomycin is associated with neutropenia in some normal people[10].

Biopsy should be considered when a skin nodule develops in a neutropenic patient, since histologic identification and positive bacterial or fungal cultures may precede development of a positive blood cultures for the infecting agent. These patients may also present without purulent sputum or without any sputum and may not produce physical findings suggestive of chest consolidation[10].

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Neutropenic patients are also predisposed to the development of invasive fungal infections, most commonly *Candida* species and *Aspergillus* others are, *Fusarium*, *Trichosporon*, and *Dreschlera*. *Cryptococcus* infection, which is common in patients on immunosuppresive agents and those with AIDS, is uncommon in patients receiving chemotherapy for acute myelogenous leukemia.

Bone marrow transplantation for either immune deficiency or cancer results in a transient state of complete immune incompetence. Immediately following transplantation, both phagocytes and immune cells (T Cells and B Cells) are absent, and the host is susceptible to infection. The reconstruction that occurs following transplantation has been likened to the maturation of the immune system in neonates[11]. The analogy does not entirely predict infections seen in these patients, however, because the new marrow is usually expressed in an old host who has several latent infections already[11].

The organisms that cause infections in these patients are different from those in bone marrow transplant recipients because solid organ recipients do not go through a period of neutropenia. On the other hand, since organ transplant patients are immunosuppressed for more prolonged periods (usually permanently), they are susceptible to the same organisms as cancer patients with impaired T cell

immunity. Also since the transplantation procedure involves surgery, the recipients are subject to wound infections[11].

Pathophysiology of hospital acquired infections

The risk of contamination leading to infection is increased if the organisms can multiply within the medical equipment. This requires moisture, because no bacteria or fungi will grow in a totally dry system, the nutrient content and temperature of the available fluid largely determining which organism will survive and multiply. In general Gram-positive bacteria such as staphylococci require near-physiologic fluid, whereas many of the Gram-negative rods are much less demanding. Even with proper growth conditions, many hours are required before contaminating organisms become numerous. The risk of infection begins to increase after 24 - 48 hours and is cumulative even if the device is changed or disinfected at intervals. The infection risk of a single urinary catheterization has been estimated at 1- 5%. Indwelling catheters carry a risk that may be as high as 10% for each day the catheter is in place[12]. Needles and plastic catheters placed in veins (or less often, in arteries) for fluid administration, monitoring vital functions, or diagnostic procedures are a leading cause of nosocomial bacteremia. Machines that assist, or control respiration by pumping air directly into the trachea have a

great potential for infection if the aerosol they deliver becomes contaminated. Hence patients admitted to the ICU have a 5 – 10 fold higher risk for developing nosocomial respiratory infection than in any other hospital ward[12].

Surgical wound infections

Patients who are admitted to hospital for surgical operations risk acquiring one or more nosocomial infections. Surgical wound infections account for 25 to 30 percent of nosocomial infections[11]. Surgical procedures have long been classified as clean, clean-contaminated, and dirty-infected. The risk of wound infection, varies from 2.9 percent for clean procedures to 12.6 percent for already infected sites.

Assessing the risk of wound infection employs an index which uses abdominal operation, surgery lasting more than two hours, contaminated or dirty-infected surgery by the classic wound classification system, and the presence of three or more diagnoses in the patient and predicts wound infection rates between 1 and 27 percent[11]. Other risk factors for the development of postoperative wound infection include the presence of a drain; preoperative length of stay, with rates doubling for each week of extra preoperative

hospitalization; perioperative shaving of the field, especially 24 hours or more before the procedure; length of surgery; presence of untreated remote infection; and the surgeon.

Preoperative antibiotic prophylaxis has been shown to decrease wound infection rates in a number of studies, including those of clean surgical procedures. Antibiotic coverage after surgical wound is closed has not been shown to provide additional benefit[11]. Pathogens that infect surgical wounds can be part of the patient's normal flora (endogenous source) or acquired from the hospital environment, other infected patients or the patient's attendees (exogenous source). Endogenous sources appear to be responsible for most postoperative infections especially if clean operations are excluded[13].

The role of antimicrobials on ICU acquired nosocomial infections

Antibiotic therapy, by reducing competing flora, may create a predisposition to hospital-acquired infection often with resistant organisms. Many patients will receive broad spectrum antibiotics that alter the endogenous bowel flora resulting in loss of colonisation resistance, partially due to antimicrobial pressure[14,15]. Antibiotic resistant organisms, usually gram negative bacilli or yeasts, can then colonise the mucous membranes and predispose to respiratory,

urinary and wound infections.

Resistance to antimicrobial agents is an evolving process, driven by the selective pressure of heavy antibiotic use in individuals living in close proximity to others. The ICU, crowded with debilitated patients who are receiving broad-spectrum antibiotics and who are cared for by busy physicians, nurses, and technicians, serves as an ideal environment for the emergence of antibiotic resistance. These pathogens include multiply resistant gram-negative bacilli, methicillin-resistant *Staphylococcus aureus* and the recently emerged Vancomycin-resistant enterococci[16].

In intensive care units, the prevalence of strains multiresistant to many antimicrobial agents is higher than in other hospital units[14,15]. Over 80% of patients in the ICU receive antibiotics during their stay and the routine use of a single broad spectrum antibiotic is likely to result in a rising prevalence of infection by resistant bacteria[17].

Antibiotics such as ampicillin, imipenem or cefoxitin are potent inducers of beta-lactamase in gram-negative bacteria and resistance to cephalosporins may persist after treatment is completed[18]. In such cases a combination of antibiotics with the specific intention of widening the spectrum, providing synergistic activity, and

discouraging the emergence of resistance during treatment is advocated[18].

The continuous bacterial adaptation to the antimicrobial pressure by the development of antimicrobial resistance mechanisms emphasises the need for new antibiotics which are active against micro-organisms resistant to previously used antibiotics (older derivatives). This should be done together with judicious use of antibiotics in the treatment of bacterial infection[19,20].

Equipment and medical staff

Organisms from asymptomatic patients readily contaminate bedpans, floors and the hands of staff. The most likely route of cross infection is via hands of nurses, physiotherapists, and other medical staff. It has been reported that, doctors wash their hands only after 28% of contacts with patients, nurses after 43% of contacts, and physiotherapists after 76% of contacts[21]. Yet hand washing is the single most important means of preventing the transfer of infectious agents, and when rates of appropriate hand washing increases, the incidence of nosocomial infection among patient populations decreases[22].

Despite recent advances in the field of medicine, surgery and better antibiotics, bacterial infections and/ or sepsis remains one of the leading causes of morbidity and mortality. In modern intensive care units, more seriously sick patients are treated more aggressively. Patients housed in ICUs have been described as "exquisitely susceptible" to infection because their natural defence mechanisms are impaired as a result of underlying diseases, extremes in age, medical and surgical interventions, and because they occupy an environment in which frequently used antibiotics ensure the survival of common nosocomial pathogens. Furthermore the close proximity of patients in many ICUs facilitates transfer of organisms from patient to patient, and that transfer is too often facilitated by the unwashed hands of health care providers[22]. In these patients life threatening sepsis with associated organ failure may be as high as 30%[23]. This may lead to cross infections between patients, particularly when the pressure of work leads to breakdown of aseptic technique. The rates of infection in ICU, vary between 7 and 45 percent and this rate increases with the duration of stay in the unit[24].

Intravascular catheters are a potential source of bacteremia in intensively monitored patients. In one study the prevalence of bacteremia increased with the duration of use of intravenous

catheter. However, it varied with different areas of the body; when femoral vein was used the prevalence was 29%, compared with the 13% when using the subclavian vein[25,26]. Bacteraemia from arterial cannulae is rare.

Multiple trauma patients with open wounds or burns are highly susceptible to infections with bacteria from the environment or from the patient's own flora, particularly if they require assisted/mechanical ventilation and/or have impaired airway reflexes[27]. In one study 81% of patients developed infection during a mean stay of 14 days in the ICU[15]. These included respiratory tract infections in 59% of cases, septicaemia in 42%, urinary tract infections in 32% and wound infections in 25% of patients[17].

The great epidemics of past centuries are now controlled through massive immunisation programmes, better hygiene, and better nutrition. The early enthusiasm with the use of antibiotics has been replaced with the realisation that, although they are important adjuncts in the treatment of infections, they are not the ultimate answer[28].

The pathophysiology of septic process

If further progress is to be made in the control of morbidity and mortality from infection, the biology and pathophysiology of the septic process must be understood in order to make a rational, systematic approach to treatment modalities. The determinants of infection can be divided into three major components:

i. The micro-organism producing the infection,

ii. The environment (local factors) in which the infection is produced,

iii. The host defence mechanisms.

There is a continuous, dynamic interaction among these factors that represent the state of homeostasis which is a balanced interaction between the three determinants.

The opposite situation, where most if not all the determinants are altered, can be seen in patients treated in the intensive care units. The patient is greatly threatened by sepsis, exposure to many pathogenic, antibiotic resistant organisms, in the setting of environmental (local defences) alterations (catheters, drains, open wounds) and altered host defences.

The first two determinants of infection, the environment and bacteria

have been extensively investigated. The environment is manipulated through practising principles of antisepsis and asepsis. In the case of bacteria even rational use of antibiotics, although proven helpful, is just a partial solution. Often the rational or irrational use of broad spectrum antibiotics may induce an ecological vacuum in the host's normal bacterial flora that is soon replaced by opportunistic and more virulent pathogens. Currently sepsis is approached mainly through the first two, environment and bacteria[29].

In a surgical patient bacterial infections are more frequent compared to viral and parasitic infections, which are much less frequent, and fungal infections are significant only in the severely immunocompromised patients. The systemic response to sepsis is not only secondary to a direct effect of bacteria on the host but also due to the host's response to micro-organisms.

There are three manifestations of bacterial sepsis: the acute, the chronic, and the toxigenic, and to the intensivists/surgeon the acute type is the most important. Such infections are caused by, nosocomial gram-positive and gram-negative bacteria. Bacterial sepsis is characterised by fever, chills, obtunded mental status, and a general feeling of malaise. In the very old, neonate or immunocompromised patient, a change in mental status or general

well being may be the only clue to a septic process[28].

Sepsis accompanied by immunologic, haemotologic and metabolic changes- termed as the acute phase response, is mediated by the host in response to an invading micro-organism. It mobilises 'host resources' in an attempt to 'localise', control, and if possible eradicate bacteria, it is a dose-graded response; bacteria and bacterial products such as endotoxins are the most potent inducers. Central to this response is the macrophage and its equivalent cells in the skin, interstitial tissues, lung and the reticuloendothelial system, these secrete IL-1 when induced by bacteria and its products[28].

During sepsis, there is a rapid shift in metabolism toward the production of acute- phase reactants and an associated body protein catabolism to provide the energy and amino acid building blocks required[30]. The body stores of protein most affected are initially the skeletal muscles and albumin, and subsequently systemic organ proteins.

The objective of the acute phase response is to recruit and deliver immunologically competent leukocytes and associated humoral factors. There is also mobilisation of the host's metabolic processes important to immune cell function in order to localise the invading

micro-organisms. Failure to localise the invading organisms results in the continued illness as witnessed in a patient with an undrained intra-abdominal abscess. This will also, result in the dissemination and continued stimulation of the acute phase response, dissemination of stimulated leucocytes and self mutilation of the host. Continued metabolic catabolism and indiscriminate release of proteases and oxygen intermediates by stimulated polymorphonucleocytes (PMNs) becomes a vicious cycle that leads ultimately to progressive organ failure and death[31].

It is likely that the true incidence of sepsis has been underestimated. In most cases of sepsis there is an underlying disease or condition which could be mistaken as the cause of morbidity or mortality; however many of these sepsis cases are associated with healthcare practices and the vast majority of these occur in hospital setting[32].

In the hospital, several situations have been associated with the development of sepsis. Any procedure that involves the possibility of infection has the risk of causing sepsis; i.e. the use of invasive devices may damage internal membranes, while the device itself may serve as a focal point of infection. A large percentage of intensive care unit patients are post operative, and this also in many places has the largest group of septic patients.

The risk factors for ICU acquired infection are increasing length of ICU stay (>48 hours), diagnosis of trauma, central venous catheterisation, pulmonary artery catheterisation, and urethral catheterisation. Others are absence of infection on admission, age >60 years, mechanical ventilation especially in situations where there is more than one intubation, and a prior episode of gastric content aspiration.

Mechanical ventilation of more than 3 days, presence of obstructive pulmonary disease, the use of positive end expiratory pressure during mechanical ventilation, have also been identified as risk factors. Age under six months, children with endotracheal intubation, the depression of the patient's level of consciousness and the horizontal position of the head and an admitting diagnosis of burns. Last but not least the risk factors include trauma, central nervous system disease, respiratory disease, cardiac disease, and the use of paralytic agents[15,33,34,35,36].

Moreover the increasing use of immunosuppresants such as corticosteroids, chemotherapy, radiation and antirejection therapy has contributed to the trend of an increased incidence of sepsis in hospital settings.

Certain acute conditions have been associated with physiological states akin to shock; these include pancreatitis, fat embolism, haemorrhagic shock, ischaemia and various forms of trauma that result in tissue injury. Chronic conditions that compromise the immune system can also increase the risk of sepsis; these include cancer, human immunodeficiency virus infection and diabetes[37].

As said above the underlying cause of sepsis usually involves some form of bacterial infection. Before antibiotics were in common use, it often resulted from a gram-positive bacterial infection, especially of the streptococci or staphylococcus species. With the powerful broad-spectrum antibiotics available today, sepsis often results from nosocomial gram-negative infection. The rising incidence of sepsis, and sepsis related deaths, may result from wrong healthcare practices.

Renovation of ageing hospitals increases risk of airborne fungal and other infections[38]. The shift to outpatient care is leaving the most vulnerable patients in hospitals. The pooling of patients in hospital, leads to a concentration of various susceptible hosts who would be cared for by the hospital staff and equipment which could cntaminate them with virulent strains of pathogenic organisms found the

hospital environment, which could not have occurred if these patients were cared for in their homes. With new medical and surgical techniques being implemented, the risk of accidental infection increases. Recent advances in management of critically ill patients, such as the use of indwelling devices such as surgical prostheses, intubation equipment, vascular and urinary catheters may abrase interior body surfaces, resulting in small openings where bacteria may gain entry, thereby creating a cohort of particularly susceptible persons. At the same time those devices may also act as a focal source of infection.

Contaminated intravenous fluids have been shown to be the cause of many cases of bacteremia. In the 13 years after 1964, 33 epidemics were caused by such an event (that is, contamination of intravenous fluids)[39]. Contamination of commercial products by gram-negative bacilli was shown to be the cause in 80% of these epidemics[32,39].

At the same time the improved ability of physicians to support patients through serious medical situations has also caused an apparent increase in the number of sepsis cases[32].

Sepsis is a serious medical condition capable of killing the patient abruptly. The use of antibacterial agents presumes that the aetiology

is bacterial and in the majority of instances this will be the case but the possibility of other causes such as fungi and viruses cannot be ruled out. In instances where bacterial infections are suspected the cause of the infection will be either a gram-positive or gram-negative organism and one that is normally part of the patient's own bacterial flora.

In one study it was observed that the identification of *Staphylococcus aureus* nasal carriers on admission may be particularly useful in identifying those patients who are at high risk for developing staphylococcal infections during their ICU stay[40]. Patients with methicillin resistant *Staphylococcus aureus* [MRSA] infections are less likely to survive than those which are sensitive to methicillin[41]. In another study it was shown that patients with perioperative MRSA nasal colonisation were at significantly increased risk of subsequent postoperative MRSA infection[42,43]. Also, there has arisen suspicion that the typical flora identified with various infective episodes are derived from the gastrointestinal tract.

The oropharynx of hospitalized patients can become colonized by many species of aerobic gram-negative organisms within 48 hours of hospitalization[11]. Micro aspiration occurs commonly during sleep and is increased by such factors as a nasogastric tube, altered

consciousness, decreased gag reflex, or delayed gastric emptying, which have been implicated as a major cause of hospital acquired pneumonia and such secondary infection can be prevented with oral, non absorbable antibiotics[45].

In recent years, the role of gastric colonization has been recognised. Bacterial counts in the stomach rise in the presence of medications that alter gastric pH, those that raise it, such as H_2 blockers and antacids, as well as in the malnourished, achlorhydric, or some elderly patients[11], tend to encourage bacterial overgrowth, as the low pH is not favourable for their growth. Gastric colonization is believed to influence development of pneumonia by retrograde colonization of the oropharynx.

Early treatment with antibiotics, started before the causative organism has been isolated and cultured, has been shown to improve the antibiotics effectiveness[46]. Early treatment is of particular importance in immunocompromised patients where delaying treatment for 24 hours may result in the death of the patient. The immediate empirical use of parenteral, broad-spectrum antibiotics is recommended whenever infection and sepsis are suspected[46,47]. In many instances, however, a causative organism will not be identified, thus in the early phase of treatment the choice of antibiotic is based

on the known antimicrobial susceptibility of common bacterial pathogens in a particular hospital, the type of organisms most frequently associated with sepsis are often characteristic of a given hospital[47].

The correct choice of antibiotics usually centre around the following factors:

- Likely pathogen(s) and their antibiotic susceptibilities,
- Underlying condition and immune system status of the patient,
- Antibiotic pharmacokinetics
- Cost-effectiveness

In order to provide rapid bactericidal activity against suspected pathogens it is advised to use a combination of antibiotics. Other reasons for administering combinations of different antibiotic classes is to decrease the likelihood that a resistant population of bacteria will emerge during treatment and the additive effects, or possible synergy, obtained from combinations of rapidly bactericidal agents. The simultaneous use of synergistic agents has been associated with a better clinical result in bacteremia[48].

In spite of the availability of many potent agents, there are few controlled clinical trials showing differences between regimens for the

treatment of sepsis with newer agents, in appropriate doses. A frequently used combination of antibiotics is a third -generation cephalosporins like ceftriaxone, ceftaxidime or cefotaxime plus an amino glycoside, for example gentamicin or amikacin. All these have been found to have good activity against many of the organisms responsible for sepsis and have been shown to be effective in non-neutropenic patients[29].

Ceftriaxone has a long half -life and can be administered on a once-daily basis; the others have shorter half-lives and must be administered daily using a multiple-dosing regimen. For neutropenic patients, a penicillin with enhanced activity against *Pseudomonas aeruginosa* e.g. Mezlocillin, in combination with an aminoglycoside administered several times daily as an effective treatment for a hospital -acquired infection. Imipenem, a carbapenem, has also been used successfully in the treatment of sepsis[49]. More studies with sufficient patient numbers are needed to determine the optimum antibiotic therapy for patients with sepsis.

Some work has focused on the once-daily administration of aminoglycosides as a way of reducing toxicity. In one study ceftriaxone, administered once daily was combined with netilmicin given either once daily or in conventional multiple daily-dosing

regimens in a group of elderly patients with severe bacterial infections[50]. In that particular study, it was found that once-daily dosing with an aminoglycoside plus a long acting cephalosporin was a cost-effective and safe treatment for severe bacterial infections. In another trial, once-daily dosing with a combination of amikacin and ceftriaxone was compared with ceftazidime and amikacin given three times daily[51]. All of the 694 patients from 21 centres were febrile and neutropenic. There was no statistically significant difference between the two regimens either in terms of overall response (71% and 74%) in the ceftriaxone and ceftazidime groups, respectively, or in the incidence of toxicity[50].

Where the causative pathogen is identified the choice of antimicrobial agent is guided by the antimicrobial sensitivity pattern of the particular pathogen. The use of monotherapy coupled with use of a narrower spectrum of activity, is good clinical practice and often leads to the control of infection.

Ceftriaxone, is the first cephalosporin with a very long half-life which permits effective once-daily dosage. This feature together with a broadspectrum of activity and good tolerability may give ceftriaxone great deal of clinical utility[52].

The wide range of antibiotics available today makes it imperative to decide which drugs should be included in the hospital formulary. In addition to efficacy and low toxicity, cost containment is a major issue, so factors determining the choice of a third generation Cephalosporins are:

Broad spectrum of activity,

Long half-life to permit infrequent dosing,

Relative absence of serious or life threatening side effect,

Cost effectiveness, it is not merely the acquisition costs of an antimicrobial agent which determine the cost of therapy, a number of other factors have to be taken into account such as delivery costs, time needed by nurses, pharmacists and technicians and hardware necessary to administer an intravenous drug. To this the cost of complication due to toxicity also must be added. The true cost of an antibiotic can be estimated by apportioning the cost relative to the dose or per day of therapy.

The change from cefotaxime to ceftriaxone has not been found to have any impact on outcome from a clinical and microbiological point of view[51]. When 2g ceftriaxone every 24 hours is substituted for 2g cefotaxime every 8 hours, therapy appears to be about 10 -15% less expensive. However for a variety of infections 1g ceftriaxone once daily is sufficient. If the cost of this regimen is compared with

traditional doses of antibiotics used, there is a substantial cost difference of between 20 and 100US dollars per day of therapy[51]. A continuous monitoring of antibiotic policy that uses drugs that are administered less frequently, based on their pharmacokinetics, can lead to appropriate patient care and be cost effective

PART II CLINICAL STUDY

Introduction and rationale:

The Intensive care unit at Muhimbili Medical Centre is situated below the main operating theatre between the Casualty department and general wards. There are eight beds, to each bed there is an oxygen source and suction apparatus, four mobile suction machines and one, foot operated suction pump, there are three wash basins, two cardiovertors, eight monitors (Datascopes), two infusion pumps, and five ventilators, airways of various sizes, endotrachea tubes, nasal prongs, face masks, and venti masks. And a variety of resuscitation, cardiac support, renal support drugs, such as Atropine, Adrenaline, Thiopentone Sodium, Suxamethonium Chloride, Pancuronium Bromide, Diazepam, Midazolam, Dopamine, Dobutamine, Hydrocortisone, etc. There are three airconditoners, two sluice rooms, an office, and an equipment store, which serves as a changing room as well. It is a multidisciplinary unit, which cares for medical, surgical, paediatrics, gynaecological, orthopaedic and trauma patients, whose commonest hospital acquired infections as in any other Intensive care unit are urinary, respiratory and systemic infections as complications.

Urinary tract infections (UTIs) are the most common hospital acquired infections, accounting for about 40 to 45 percent of all nosocomial infections and generally are the easiest to treat with the least severe sequelae. Pneumonia accounts for 15 to 20 percent, and bacteremia, mainly associated with intravascular devices, 5 to 7 percent most patients dying in the ICU, have at least one episode of infection, pneumonia accounting for more deaths than infection at any other site.

Specific risk factors and common pathogens that causes nosocomial infections in our ICU are not known, and have not been studied before, as a result, specific measures for the prevention of these nosocomial infections cannot be instituted with certainty. Thus it was of interest to determine such factors including carriage of potential pathogens among medical staff, patients and contamination of equipment.

In addition, the of antimicrobial susceptibility pattern of the causative bacterial pathogens identified in our patients is not known but is necessary in order to assist in making rational clinical decisions on therapeutic intervention.

Members of staff and equipment utilized in patient care have been suspected of harbouring pathogenic micro-organisms. This

component has not been worked on hence the need to determine the types of such organisms and their antimicrobial susceptibility pattern.

OBJECTIVES

BROAD OBJECTIVE:

To determine the prevalence of nosocomial infections, associated risk factors, and the antimicrobial susceptibility pattern of bacterial infections acquired during ICU admission.

SPECIFIC OBJECTIVES:

i. To determine the prevalence of nosocomial infections among patients admitted in the ICU, MMC.
ii. To determine the carrier role for potentially pathogenic bacteria among regular medical staff working in the ICU.
iii. To determine the knowledge, attitude and practice of ICU nurses and doctors on possible causes/sources of nosocomial infections.
iv. To determine the sterility of equipment used in the ICU.
v. To determine the efficacy of the sterilising/cleaning agents for ICU equipment.
vi. To determine the antimicrobial susceptibility pattern of common bacterial pathogens isolated from patients, medical staff and

equipment in the ICU at MMC to various antibiotics.

vii. To determine the incidence of nosocomial pneumonia among patients using oxygen masks as compared to endotracheal intubation for invasive positive pressure ventilation.

viii. To evaluate the relationship between ICU acquired infections and mortality.

ix. To determine the feasibility of a continuous surveillance of ICU acquired infections

METHODOLOGY

STUDY AREA:

The Muhimbili Medical Centre is a tertiary health care facility, located in Dar es Salaam. The catchment area for this facility is mainly the City of Dar es Salaam with an approximate population of 3million inhabitants (in the absence of a Regional Hospital), Coast Region, and as a referral point for Zanzibar, Morogoro, Dodoma, Mtwara and Lindi regions. It also receives patients from all over Tanzania whose conditions cannot be adequately managed at their respective Consultant/and or Regional Hospitals. This institution also serves as a teaching hospital for the Muhimbili University College of Health Sciences of the University of Dar es Salaam.

The Centre's total bed capacity is about 1500 at any given time. Out Patient Department (OPD) and those contacted during Out reach, Public Health and Community services.

The Intensive Care Unit at MMC is a multidisciplinary unit. It cares for critically ill patients from medical, surgical, paediatrics, gynaecological, orthopaedic and trauma departments, and a few from other health providing institutions around the city, whose lives may be supported in the intensive care.

Three Consultant Anaesthesiologists, routinely rotate on a daily basis providing expert care needed for the patients. Postgraduate students in the department provide services under instructions from the consultants just as the Registrars, Anaesthetic officers, and Nurse anaesthetists. Nursing services, are provided by six nursing Officers, eight nurse midwives, four trained nurses, five auxiliary nurses and five ward attendants. These work in such a way that the unit is covered round the clock, some nurses work in the morning shift, others work during the afternoon, and others at night. While nurses in other departments rotate from one department to another from time to time, this rarely occurs with ICU nursing staff, and it did not occur during the study period. The nurse:patient ratio was 2:1.

There is always a Consultant anaesthesiologist on call, and a resident or an anaesthetic officer working under a consultant. Consultants and Specialists from other Departments do come to review patients admitted there from their departments. Physiotherapists are usually invited to provide exercises to some patients while Spiritual leaders of various denominations do come to offer spiritual support to the patients at the request of the patients or their relatives.

STUDY POPULATION:

There were two study populations. All patients who were admitted to the ICU over a period of 9 months. (except those who died within 30 minutes of admission), and the medical staff working in the ICU.

STUDY DESIGN:

This was a cross sectional study.

The study was carried out between May 1999 and January 2000.

SAMPLE SIZE:

The sample size was determined by using a formula designed for population surveys in cross sectional studies using EPINFO 6 computer program. The formula states that:

$$n=Z^2P(1-P)/d^2$$

where, n is the sample size

Z = Standard normal deviate corresponding to a two sided specified significance level.

P = (expected) prevalence of nosocomial infections.

d = margin or boundary of error on P.

Setting a significance level of 0.05, gives Z= 1.96

Putting P = 20.3%(0.203) and d = 6.1%(0.061) yielded a sample size, n, of 167 patients.

Since the selection of patients for the study was done from a finite population, the final sample size was thus adjusted for this. That is, the finite population correction was applied, using the following formula:

$n' = n/[1+(n/N)]$, where,

n' is the adjusted sample size.

n is the sample size obtained before applying the finite population correction.

N is the total study population from which the study sample was obtained (N = 300).

Hence, n'=107, which was the minimum calculated sample size.

- The average number of patients admitted to the ICU was 25 ± 5 per month and, as there were no seasonal variations, all patients admitted over a period of 9 months were included.

DATA COLLECTION:

Data collection was done by using a questionnaire, which was filled in by the principal investigator at the patient's admission and during the patient's stay in the ICU. The questionnaire inquired about the diagnosis for admission, the type of respiratory support needed, and the urogenital system care, also the information on the swabs taken and their results. Staff members were interviewed by the principal investigator, on their knowledge about nosocomial infections, attitude and practice, their responses were filled in respective questionnaires. Swabs from the various body sites were also collected and submitted to the laboratory.

Results from the microbiology laboratory, including the isolated pathogens and their antimicrobial susceptibility pattern were recorded.

CLINICAL AND LABORATORY PROCEDURES:

All patients admitted to the Intensive Care Unit were clinically evaluated, their socio-demographic data collected and swabs from their nares, urethral catheters and endotracheal tubes were taken. The swabs utilized were factory made with their own transport media, they were wrapped in a sterile pack which was opened at the time of

collecting the specimen. These were labelled with a name and the sites from where they were taken before being taken to the laboratory for processing. These were submitted to the laboratory for gram staining, culture and determination of their antimocrobial susceptibility pattern of bacterial isolates. Bacterial pathogens were isolated using standard laboratory media.

The antimicrobial sensitivity pattern was determined by use of routine laboratory protocols which were available at Muhimbili Medical Centre during the study period. This was Stokes method which entailed innoculating a pure culture of the bacterial isolate into an Isosens agar including a standard organism (*S.aureus or E.coli*). Antibiotic discs were placed on the innoculated culture plate with a maximum of 8 discs per plate. Plates were incubated at 37°C for 18 – 24 hours. Sensitivity pattern were read such that the organism was said to be sensitive if the test zone was obviously larger than the control or the zone radius was equal, wider or not more than 3mm smaller than the control. Intermediate sensitivity had the zone size greater than 3mm, but smaller than the control by more than 3mm. The organism was said to be resistant if zone radius was 3mm or less/ or give no zone of inhibition at all.

ROCEPHIN (CEFTRIAXONE):

Ceftriaxone (made by ROCHE) was given to some patients whose infecting agents proved sensitive to it. This was based on evidence accrued from literature on studies conducted elsewhere, which have shown a very broad spectrum in its activity against microbes, so when antimicrobial susceptibility was carried out this was included in the standard Muhimbili Medical Centre kits for the same. All those with susceptible microbes were treated, as the drug was available, during the whole course of this study.

SURVEILLANCE:

The surveillance programme included collection of swabs from specified sites in the ward for culture in the laboratory. Sites swabbed included beddings, utensils, furniture bedframes, basins, ventilator tubings, airways, endotracheal tubes, suction catheters, nasal prongs, and face masks. This was done routinely, i.e. weekly for one month then on a monthly basis for three months, swabs were submitted to the microbiology laboratory. The laboratory results provided were recorded and employed in the analysis of the situation

LIMITATIONS

1. The laboratory did not have adequate facilities with which to identify all organisms to species levels.
2. The ICU did not have in place facilities to collect the specimens, these had to be collected from the main laboratory at the Centre.
3. The laboratory had a limit to the number of specimens that could be processed in a given day, this led to missing the pathogens on admission for the specimen which could not be processed on time as a result.
4. Some staff members were resistant to suggested means that were aimed at reducing the risk of transmitting nosocomial infections.
5. Study funding was not adequate and not timely to meet all the study requirements.

RESULTS:

During the study period, May1999 to January 2000, a total of 262 patients were admitted to the ICU at Muhimbili Medical Centre. Out of these, 179(68.3%) were males and the rest [83, (31.7%)] were females (Table 1)

Table 1.**Patients admitted to the ICU during the study period**

	Males	Females	Total	
	No (%)	No (%)	No	(%)
All patients	179(68.3)	83(31.7)	262	(100.0)
Patients included	126(63.0)	74(37.0)	200	(76.3)
Patients excluded	40(90.9)	4(9.0)	44	(16.8)
Lost results	13(72.2)	5(27.8)	*18	(6.9)

There was no difference, in terms of diagnosis, care and samples submitted to the laboratory in the patients whose data could not be traced with the remainder of the patients in the study.

Sixty-two (23.7%) patients were excluded from the study due to the following reasons:

- 14 patients died within 30 minutes of admission.
- 30 patients were discharged before investigations were carried out. This was due to occasional absence of swabs and transport media.
- 18 patient's specimen/results could not be traced in the laboratory due to poor storage and at times documentation or laboratory records were mixed with those of routine

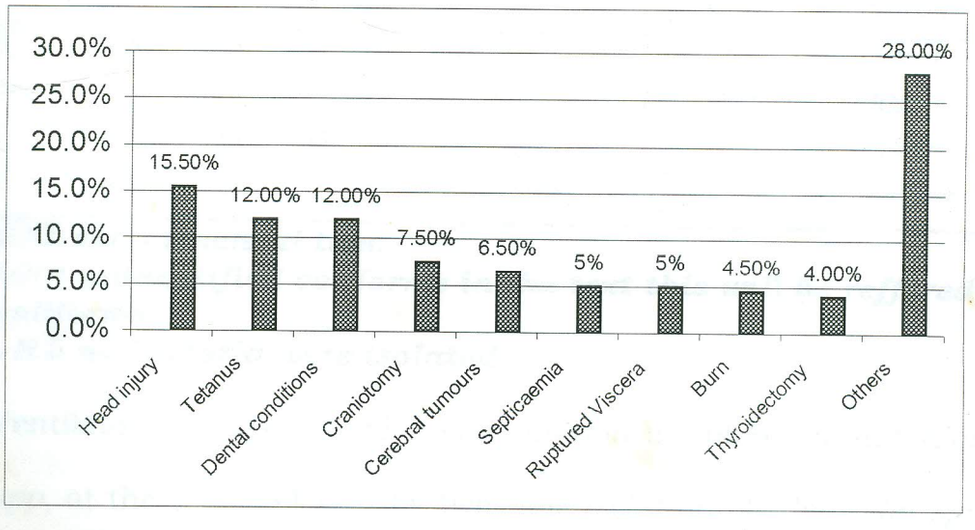
investigations from other wards where tracing became very difficult or were lost altogether.

Therefore 200, patients were involved in the study.

Table 2 shows the diagnosis of patients at admission to the ICU.

Table 2: **Diagnosis at admission**

Patient's Diagnosis	Number(%)
Head injury	31(15.5)
Tetanus	24(12.0)
Dental conditions	24(12.0)
Craniotomy	15(7.5)
Cerebral tumours	13(6.5)
Septicaemia	10(5.0)
Ruptured Viscera	10(5.0)
Burn	9(4.5)
Thyroidectomy	8(4.0)
Others(CCF,D.melittus,Renal failure)	56(28.0)
Total	200(100)



The leading cause for admission, to the ICU at Muhimbili Medical Centre, during this study was head injury, which accounted for 15.5% of patients, followed by tetanus, which accounted for 12% of

cases. The rest of the diagnoses such as congestive cardiac failure, amputees [suffering from complications of diabetes mellitus or from extensive multiple injuries], patients with chronic renal failure, severe cardiac disrhythmias, acute lymphocytic leukemias, gastric malignancies, cerebral vascular accidents, complications following caesarean section, multiple trauma, respiratory distress syndrome, surgical emphysema, who required some form of ICU care made up 28% cases.

The commonly isolated organisms from ICU equipment at three months intervals were as shown in Table 3.

Table 3: **Prevalent bacterial pathogens in the ICU equipment:**

TIME	BEDS	Beddings	Ventilator. tubings	Airway	ETT	Suction. Catheter	Nasal. Prongs	Mask
0	*UCI	UCI	Klebsiella	Bacillus spp	UCI	UCI	Bacill spp	Bacillus spp
3	S.epide	UCI	Klebsiella	Pseudomons	UCI	Klebsiella	UCI	Klebsiella
6	S.aureu	UCI	Klebsiella	Klebsiella	UCI	Pseudomons	Pseudomon	Klebsiella
9	Klebsiell	UCI	Pseudomons	Pseudomons	♦N.b	Klebsiella	Pseudomon	Klebsiella

ETT endo tracheal tube
****UCI unidentified coliforms in the text this will be reffered to as coliforms.***
♦N.b no bacteria were isolated

Ventilator tubings yielded a combination of coliforms and *Klebsiella spp,* at the start followed by two-time isolation of *Klebsiella spp,* and finally *P.aeruginosa.* Airways yielded *Bacillus spp, P.aeruginosa, Klebsiella spp, and P.aeruginosa* at the start and three months interval thereafter. The endotracheal tubes yield at three consecutive

times coliforms and the last sample yielded no bacterial growth. The suction catheter had coliforms, *Klebsiella spp, P.aeruginosa, and P.aeruginosa* at the start of the study, third, sixth, and ninth month respectively. Nasal prongs had *Bacillus spp,* Coliforms, *P.aeruginosa, P.aeruginosa* at the study, third, sixth, ninth month respectively.

The forty two medical staff, (doctors and nurses) working in the ICU, were interviewed in relation to their knowledge, attitude and practice, on nosocomial infections.

It was generally found that their knowledge on the definition of nosocomial infections was inadequate and the terminology strange to most (76.2%) of them, at first sight most thought it was the patient's admitting diagnosis. But on elaborating the meaning, a good number 30 (71.4%) managed to correctly pin point several diseases which indeed can be acquired in the ICU/hospital setting. All staff members did point out, the fact that hospital acquired infections are a problem in our set up. Low immunity, infected staff members, unsterile equipment and failure of asepsis in invasive procedures, contaminated water, unclean hands, patients overcrowding, and ignorance were pointed out as risk factors for transmitting and or acquiring infections in the hospital.

Unavailability of running water and lack of facilities for handwashing, were pointed out as the main reasons for ICU workers not washing their hands regularly. When asked why they did not follow the scrubbing protocol while washing their hands (whenever there was water) 23 (54.8%) said they were scared of bruising their hands, and others said they were too busy working to find time to do that. When asked why they did not use antiseptics while washing their hands, skin irritation scared most workers.

On the subject of wearing masks while working, 18 (42.9%)said they had none, and the few who had said they only had one piece which had been worn out, yet some acknowledged negligence. When asked why they did not ask for alternative responsibilities or duties when they were suffering from contagious diseases, they all (40) responded by saying lack of manpower in the unit forced them to continue working even though they were sick.

On failure to limit the number of visitors coming to see patients in the unit, this was due to the absence of clear guidance or regulation on the number of visitors per patient.

On why they ate, changed clothes, applied cosmetics and toiletries in

the unit, the workers pointed out that unavailability of specified room for such activities made them improvise and that resulted in what they were currently doing.

Suggestions put forward in preventing hospital-acquired infections in the unit were:

1. Provision should be made for the kitchen, dinning and changing rooms, preferably outside the unit.
2. Water supply system should be improved to ensure its availability all the time and wash-basins with soap dispensers should be conveniently placed in the ward.
3. Masks should be made available in the unit.
4. Health education should be provided on a regular basis
5. Visitors to patients should be limited to a maximum of 3 per patient during the stay, but there should only be one visitor per patient at time.

The medical staff working in the ICU, were found to harbour certain potentially pathogenic micro-organisms, particularly in the nares and axilla. There was no intervention. The most common organism isolated at three month intervals are shown in Table 4.

Table 4: **Most prevalent bacterial pathogens among 42 regular medical staff working in the ICU**

TIME	(n)	AXILLA	(%)	NARES	(%)
0	(40)	*S.epidemidis*	(62.5)	*S.aureus/ P.aeruginosa*	(80.0)
3/12	(28)	*S.epid/Kleb*	(75.0)	*S.aureus/ P.aeruginosa*	(75.0)
6/12	(34)	*S.aureus*	(50.0)	*UCI/S.aureus*	(87.5)
9/12	(36)	*S.aureus*	(67.5)	*S.aureus/UCI*	(82.5)

Kleb Klebsiella spp

****n was not constant as the workers were not all the same. This depended on their working session allocation that week in the duty roster, and others were on leave.***

Where at the start of the study most staff members harboured *S.aureus* and *P. aeruginosa* in equal numbers from the nares. Three months later *Klebsiella spp,* were isolated from the axilla while *S.aureus* and *P.aeruginosa* were isolated from the nares. At six months *S.aureus* was isolated from the axilla, and *S.aureus,* and *Klebsiella spp* were isolated from the nares. At nine months *S.aureus* was isolated from the axilla and coliforms and *S. aureus* were isolated from the nares.

The efficacy of various disinfecting agents for ICU equipment was tested, these are mainly solutions such as Lysol, Savlon, and Dettol. Swabs were taken for microbiology cultures from containers that kept these solutions. These containers are also used for soaking and

cleaning equipment utilized in patients care after each procedure. These swabs were obtained at three months intervals and all yielded no bacteria growth. However there were no efforts used to neutralise the disinfectant when processing the samples.

The antimicrobial susceptibility pattern of common bacterial pathogens isolated from patients, medical staff and equipment to various antimicrobial agents was determined and the results were as shown in Tables 5 i, ii, iii and iv[*which shows a list of second line drugs, that are sometimes employed in antimicrobial susceptibility pattern to organisms isolated in our environment*]. For each drug tested a sensitivity and resistance result was recorded. Table 5a,i,ii,iii,iv, shows confidence intervals for each of the results.

Table 5: **The antimicrobial susceptibility pattern of bacterial isolates**

i. GRAM POSITIVE ORGANISMS:

Organism	Penicillin G		Erythromyicin		Tetracycline		Cloxacillin	
	N	(%)	N	(%)	N	(%)	N	(%)
S.aureus	87	(8)	81	(58)	42	(62)	55	(96)
S.pneumococcus	3	–	3	(34)	3	(34)	2	–

Empty(–) cells no tests were done

ii. GRAM NEGATIVE ORGANISMS:

Organism	Tetracycline		Ampicillin		Chloramphenicol		Augmentin		Gentamyicin	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
E.coli	50	(50)	76	(32)	56	(71)	57	(49)	70	(73)
Proteus.spp	15	(40)	40	(25)	36	(28)	32	(68)	56	(75)
Kleb.spp	90	(64)	188	(18)	116	(45)	176	(76)	190	(81)
Coliforms	6	—	5	—	16	(37)	16	(27)	16	(75)

Empty(—) cells no tests were done

iii. *Pseudomonas aeruginosa*:

Gentamycin	
N	(%)
113	(97.3)

Also the isolated organisms were at times subjected to sensitivity tests with second line antibiotics, the results for such tests are:

iv. SENSITIVITY AGAINST SECOND LINE DRUGS:

Organism	Ceftriaxone		Ceftazidime		Ciprofloxacin	
	N	(%)	N	(%)	N	(%)
E.coli	61	(78.7)			10	(60)
Proteus	44	(100)				
Klebsiella	154	(93.5)	12	(83)	2	
P.aeruginosa	98	(93.5)				
Coliforms	12	(66.7)				

Empty cells no tests were done

Table 5a. **The antimicrobial susceptibility pattern**

i. GRAM POSITIVE ORGANISMS:

Organism	Penicillin G (%) 95% CI	Ethromycin (%) 95% CI	Tetracycline (%) 95% CI	Cloxacillin (%) 95% CI
S.aureus	8 (3.3-15.9)	58 (46.5-68.9)	62 (45.6-76.4)	96 (87.5-99.6)
S.pneum	3	3	3	2

ii. GRAM NEGATIVE ORGANISMS:

Organism	Tetracycline (%) 95% CI	Ampicillin (%) 95% CI	Chloramphenicol (%) 95% CI	Augmentin (%) 95% CI	Gentamycin (%) 95% CI
E.coli	50 (35.5-64.5)	32 (21.7-43.4)	71 (57.8-82.7)	49 (27.7-54.2)	73 (56.2-78.9)
Proteus spp	40 (16.3-67.7)	25 (12.7-41.2)	28 (14.2-45.2)	68 (63.6-92.8)	75 (61.6-85.6)
Kleb spp	64 (67.8-85.9)	18 (12.9-24.3)	45 (35.6-54.3)	76 (69.1-82.2)	81 (74.6-86.4)
Coliforms	0 (54.7-100.0)	0 (0.0-52.2)	37 (15.2-64.6)	27 (15.2-64.6)	75 (47.6-92.7)

iii. Pseudomonas aeruginosa:

Gentamycin (%) 95% CI
97.3 (92.4-99.4)

iv. ANTIMICROBIAL SUSCEPTIBILITY PATTERN FOR GRAM NEGATIVE ORGANISMS AND SECOND LINE DRUGS

Organism	Ceftriaxone (%) 95% CI	Ceftazidime (%) 95% CI	Ciprofloxacin (%) 95% CI
E.coli	78.7(66.3-88.1)		60(26.2-87.8)
Proteus spp	100(92.0-100)		
Klebsiella spp	93.5(88.4-96.8)	83.1 (88.4-96.8)	2
Pseudomonas spp	93.5(87.1-97.2)		
UCI	66.7 (34.9-90.1)		

Among *S.aureus* strains 53(96%), 7(8%) were sensitive to Cloxacillin), and Penicillin G respectively. *S.pneumonia* was isolated in a few cases, one out of three was sensitive to Tetracycline and Erythromycin, and two isolates of the three tested were sensitive to Cloxacillin while all three isolates were resistant to Penicillin G. Among the *E.coli* isolates, 48/61(78.7%), 48/70(73%), 6/10(60%) 40/56(71%), 32/76(24%) were sensitive to Ceftriaxone, Gentamicin, Ciprofloxacin, Chloramphenicol and Ampcillin respectively. Among the *Proteus* species, 100%, 42/56(75%), 26/32(68%), 10/40(25%) were sensitive to Ceftriaxone, Gentamycin, Augmentin, and Ampicillin respectively. Of the *Klebsiella spp* isolates, 144/154(94%), 10/12(83%), 154/190(81%), 134/176(76%), were sensitive to Ceftriaxone, Ceftazidime, Gentamycin and Augmentin respectively.. Coliforms were sensitive to Ceftriaxone 8/12(66.7%) and Gentamicin 12/16(75%). *Pseudomonas aeruginosa* was sensitive to Ceftriaxone 92/98(93.5%) and Gentamycin 110/113(95%). No sensitivity tests were carried out against *S.epedermidis* and *Bacillus spp.*

Table 6, shows the prevalence of nosocomial infections and the main agents responsible in each of the disease conditions.

Table 6: **Main agents (organisms) responsible for various infections(conditions)**

CONDITION	ORGANISMS	FREQUENCY(%)		95%Confidence intervals
PNEUMONIA	*Klebsiella spp*	48	(38.4)	29.84 - 47.52
N = 125	*P.aeruginosa*	36	(28.8)	21.05 - 37.58
	E.coli	12	(9.6)	5.06 - 16.17
	S.pyogenes	8	(6.4)	2.80 - 12.22
	S.aureus	8	(6.4)	2.80 - 12.22
	No Bact growth	13	(10.4)	5.65 - 17.13
URINARY	*Klebsiella spp*	66	(36.7)	29.39 - 44.16
TRACT	*E.coli*	38	(21.1)	15.39 - 27.81
INFECTION	*Proteus*	38	(21.1)	15.39 - 27.81
N = 180	*P.aeruginosa*	38	(21.1)	15.39 - 27.81
BACTEREMIA	*P.aeruginosa*	3	(15.0)	3.21 - 37.89
	S.epidermidis	2	(10.0)	1.23 - 31.69
N = 20	*Coliforms*	2	(10.0)	1.23 - 31.69
	E.coli	2	(10.0)	1.23 -31.69
	Proteus spp	1	(5.0)	0.13 - 24.87
	S.aureus	1	(5.0)	0.13 - 24.87
	No Bact growth	9	(45.0)	23.06 - 68.47
SURGICAL	*P.aeruginosa*	12	(36.4)	20.40 - 54.88
WOUND	*Klebsiella spp*	11	(33.3)	17.96 - 51.83
INFECTIONS	*Proteus spp*	4	(12.2)	3.40 - 28.20
N = 33	*S.aureus*	3	(9.0)	1.92 - 23.33
	No bact growth	3	(9.0)	1.92 – 23.33

Pneumonia occurred in 125(62.5%) patients, and the main agents responsible were *Klebsiella spp*, *P.aeruginosa*, and *E.coli*. Thirteen

patients (10.4%) had clinical features of pneumonia such as a cough, high body temperature, nasal flaring, intercostal recession and tachypnea but no bacteria isolated.

One hundred and eighty (90%) patients had episodes of urinary tract infections, and the agents isolated from the urine were *Klebsiella spp (36.7%), E.coli*(21.1%), *Proteus spp*(21.1%), and *P.aeruginosa* (21.1%).

Bacteremia was diagnosed in twenty (10%) of cases and the leading organism isolated was: *P.aeruginosa* 15%, while 45% of the samples submitted had no bacteria growth.

Surgical wound infection was encountered in 33(16.5%) of the patients admitted to the ICU. Of these, the following organisms were isolated, *P.aeruginosa* in *36.4%* of cases, *Klebsiella spp* in *33.3%* of the cases, and *Proteus spp* accounted for *12.2%*, of surgical sepsis.

An attempt was made to establish if there was any association between the organisms that caused diseases in the patients and those that were isolated from the healthcare providers, the results are shown in Table 6a, b, and c.

Table 6a: ***Pseudomonas aeruginosa***

P aeruginosa	Positive	(%)	Negative	(%)	Total
Medical staff	8	(19.1)	34	(80.9)	42
Patients	67	(33.5)	133	(66.5)	200
Total	76	(16.5)	167	(83.5)	242

χ^2=3.39, df=1, p=0.066

Table 6b: ***Klebsiella spp***

Klebsiella spp	Positive	(%)	Negative	(%)	Total
Medical staff	10	(23.8)	32	(76.2)	42
Patients	93	(46.5)	107	(53.5)	200
Total	103	(42.6)	139	(57.4)	242

χ^2=7.31, df=1, p=0.007

Table 6c: ***Coliforms isolated***

UCI	Positive	(%)	Negative	(%)	Total
Medical staff	20	(47.6)	22	(52.4)	42
Patients	2	(1.0)	198	(99.0)	200
Total	22	(8.1)	220	(90.9)	242

χ^2=85.73, df=1, p<0.001

No significant association was found on the presence of *P.aeruginosa* in the nares of the medical staff and the finding of the same organism in the patients (***p***=0.06). A significant association was seen between the presence of *Klebsiella spp* in the nares and the isolation of these microbes from infected patients (***p***=0.007). There was a significant association between the isolation of coliforms and their occurrence in infected patients in the ICU (***p***<0.001).

Table 7 shows the type of artificial ventilation employed among patients admitted in the ICU.

Table 7: **Occurrence of pneumonia in relation to the type of artificial ventilation provided**

Mode	Nosocomial Pneumonia frequency (%)
Nasal Prong n = 39	15(38.4)
Oxygen Face Mask n = 49	20(40.8)
Endotracheal Tube n = 82	72(87.8)

One hundred seventy patients had some form of respiratory support while in the ICU. Seventy two(87.8%) of those with endotracheal tube developed pneumonia as compared to fifteen(38.4%) who had nasal prongs.

In an attempt to introduce a surveillance system in the ICU, several sites of the infrastructure and equipment, were swabbed at specified periods and cultured, and a microbial pattern obtained each time. This was followed up by a look at the number of nosocomial infections acquired by the patients who had been admitted. Table 8, shows the nosocomial infections suffered by patients during that period.

Table 8: **Feasibility of a continuos Surveillance of ICU acquired infections:**

Daily (1 month)n=30		Weekly (1 month) n=32		Monthly (3 months) n=105	
Resp	8(26.7)	Resp	10(31.3)	Resp	62(59)
UTI	12(40)	UTI	16(50.0)	UTI	90(86)
Others	10(33.3)	Others	6(18.7)	Bacteremia	39(37)
				Others	20(19)

χ^2=0.16, df=1, p=0.6911 test of significance Respiratory infections between daily and weekly sampling
χ^2=0.63, df=1, p=0.42 test of significance UTI between daily and weekly sampling
χ^2=1.72, df=1, p=0.17 test of significance Other diseases between daily and weekly sampling
χ^2=14.20, df=2, p<0.001 test of significance respiratory tract infections between daily, weekly,and monthly sampling.
χ^2=31.67,df=2, p<0.001 test of significance UTI between daily, weekly,and monthly sampling.
χ^2=3.00, df=2, p=0.12 test of significance others between daily, weekly,and monthly sampling.
Bacteremia was only noted in the three months category and not earlier.

When surveillance was done daily for 1 month a total number of 30 patients were diagnosed to be suffering from one or the other nosocomial infections. When the surveillance was carried out weekly, for one month, a total number of 32 patients were diagnosed to have the following infections. When swabbing of several sites of the infrastructure and equipment was done on a monthly basis for three months, a total number of 105 patients were cared for and the following infections were seen: respiratory (59%), urinary tract (86%), bacteremia (37%), and others (19%). No statistical significance was seen when the sites were sampled on a daily basis for one month

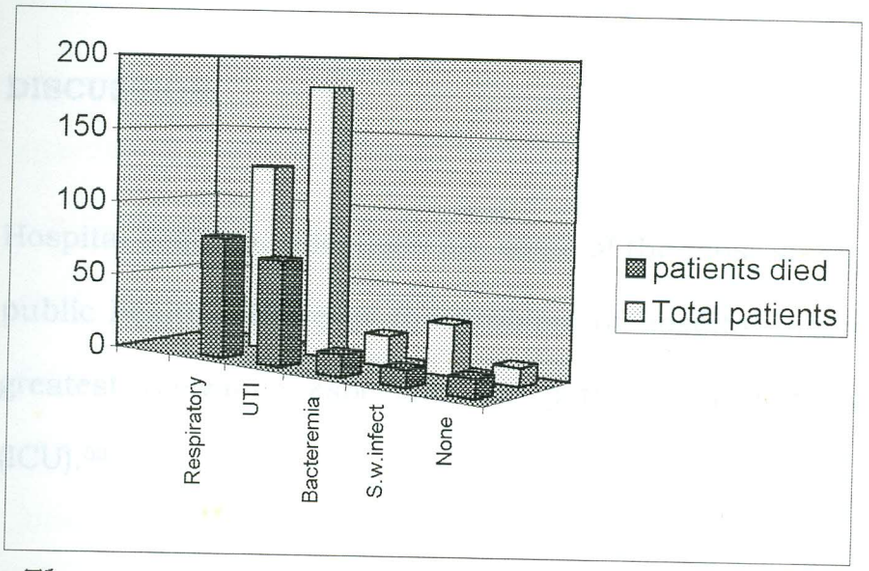
related to sampling on a weekly basis for one month (***p=0.7***). But statistical significance was seen when the daily, and weekly sampling was compared to a monthly sampling one (***p<0.001***).

Table 9, shows mortality rate among patients admitted to ICU in relation to clinical diagnosis.

Table 9: **Mortality in relation to the ICU acquired infections during the study period May 1999 and January 2000**

Type of infection	The number of patients who died	Total number of patients N	Percentage (%)
Respiratory	80	125	(64.0)
UTI	69	180	(38.3)
Bacteremia	14	20	(68.2)
SurgicalWound Infections	11	33	(33.3)
Others	12	12	(100.0)

χ^2=26.21, df=3, P<0.001., these were obtained for the defined infections and the last category (none of the above) was not included.



♦ ***There was no significant association between respiratory tract infection and bacteremia on mortality.*** χ^2 ***=0.27,df=1,p=0.6***

DISCUSSION:

Hospital acquired infections are some of the most serious problems in public health. However the problem of hospital infections assumes greatest relevance especially for patients in intensive care units (ICU).[53]

The most prevalent nosocomial infections in this study were urinary tract infections(90%), Pneumonia(62.5%), surgical wound infections (16.5%), bacteremia (10%).

The leading cause of admission was head injury (15.5%) these were mainly patients who had been involved in motor traffic accidents in the city and at times from the rest of Tanzania. This was followed by tetanus (12%) commonly admitted from medical, paediatric and surgical wards, as they usually require respiratory support once they have been paralyzed and sedated. Post craniotomy patients who are monitored in the ICU for at least 24 to 48 hours before being extubated and sent to the neurosurgical ward for definitive care and subsequent discharge constituted 7.5% of all admissions. Burn patients constituted (4.5%) of patients admitted to the ICU. While the

environment in the ICU is far from ideal for care of burn patients, in our setting, the absence of a burn intensive care unit[54], gives no alternative to the current practice, which exposes them to the risk of wound sepsis from the prevalent pathogenic organisms in the ICU such as *P.aeruginosa* and *Klebsiella spp.* Also burn patients are clearly at increased risk of infection due to the nature of the burn injury, invasive diagnostic and therapeutic procedures and prolonged hospital stay[55]

While considering the prevalent organisms in the ICU equipment, we considered those equipment sites which were prominently handled by the staff and also used by the patients while they were being cared for in the ICU. These included beds, beddings, ventilator tubings, airways, endotracheal tubes, suction catheters, nasal prongs and oxygen masks. The ideal thing was to use disposable equipment for patient care but the financial situation in Tanzania currently do not allow for that provison in our hospitals. Some of the equipment cross body defence barriers, their chances for harbouring and transmitting pathogenic organisms are high. Ventilator tubings, are conduits through which air from the ventilator is pumped to the patient's lungs, therefore any organisms that are harboured there or those that can be introduced are likely to be pumped straight in to the lungs

and there progress to cause an infection[12]. The fact that several pathogenic organisms such as *Klebsiella spp, P.aeruginosa, Proteus spp and coliforms* were cultured from these tubes points to the inefficiency of the cleansing, disinfecting and sterilising process, Merchant et al, in a study in a medical ICU in Bombay reported an extensive reuse of respiratory therapy equipment. They found a similar pattern of pathogens to be responsible for the high incidence of hospital acquired pneumonia as reported in our study[56]. Organisms which form a biofilm[4] on surfaces such as *P.aeruginosa* are possibly not affected by the various means employed for cleaning disinfecting or sterilization; therefore under favourable conditions these tend to be responsible for a large number of the hospital acquired pneumonias.

In the current study, it was found that *Klebsiella spp* were the leading pathogens that were isolated in patients who had developed pneumonia (38.8%), a finding consistent with those reported from studies elsewhere[56,57,58]. This could be explained by the organism's resistance to commonly used antibiotics, and the mucoid nature of their colonies which forms a protective cover.

E. coli was also isolated in some patients (9.6%) who had acquired

pneumonia while in the ICU, in other studies this organism is noted to be a predominant pathogen isolated in patients on artificial respiratory support and those with chronic respiratory diseases[59] *E.coli* is a gram negative enterococci that primarily inhabits the gut. Patients who were put to a ventilator following trauma, intracranial surgery, or even tetanus, and who have been paralysed, stand a great risk of being infected with gut organisms. Most of these patients are unconscious and have a nasogastric tube in place, for gastric draining or feeding. They are also prescribed with H_2 blockers to prevent stress ulcers, this leads to a rise in the gastric pH and a possible overgrowth of the gram negative enteric pathogens. When the patient's head on the bed is not raised to or above 45° which was the case in most patients encountered in this study, micro aspiration of the gastric fluid loaded with such organisms could occur[11,33,35,46,60].

The other probable explanation for the occurrence in the respiratory tract, of gram negative organisms which are found in the gut, is possibly contamination, either by the improperly washed hands of the staff caring for the patients[21,22,61,62], (**$p<0.05$**, for *Klebsiella spp* and coliforms), or direct equipment contamination during storage. This is possible to occur in our ICU, as clean equipment for various uses are kept together in open containers or heaped together in drawers, where if anything is being looked for, all others are handled as well.

In economically favourable countries these equipment are either used once, and then disposed of, or they are packed and sterilized separately before being stored in readiness for aseptic future use. The difficulty of sterilizing the equipment, in respiratory care is known[3], which calls for more research to be carried out in this area, to help combat this potential threat to life in patients who are put on ventilators[63].

S.pyogenes and *S.aureus* were also isolated in some patients who had pneumonia (12.8%), these are the traditional organisms, known to cause nosocomial pneumonia partly because they are usually resident in the nares of the patient or the nares of health care providers[3]. Few *S.aureus* isolates from these patients were tested for methicillin resistance, due to lack of appropriate reagents.

A small proportion of patients (10.4%) presented, with features of pneumonia but the culture of their sputa or bronchial secretions were negative, that is no organism was isolated, this is in agreement with previously reported studies[11,64,65]. In a certain study, one Barret-connor found that 45% of untreated patient's specimen were negative on culture when routine collection and culture methods were used. This could be explained by, inadequate specimen and uneven

distribution of micro organisms in the specimen, such that even with the best available methods a significant fraction of living bacteria fail to grow on plate culture[65]. The total viable count rarely exceeds one fifth of the total microscopic count, in mixed cultures population pressure and the antagonistic effects of products of unlike organisms could hinder microbial growth, the usual delay in transport of material to the laboratory permits overgrowth[65] of other bacteria which might not grow on the index media.

It has been documented that aspiration of oropharyngeal material with its high concentration of anaerobic bacteria has been implicated in the pathogenesis of ventilator associated pneumonia and aspiration pneumonitis[66], no single anaerobic bacteria was isolated in this study, since the laboratory tends to process specimens routinely and one has to give specific instructions where an anaerobic organism is suspected. We could also, be dealing with organisms that are not commonly known to cause pneumonia in our environment, and the routine tests in place could not pick them. Organisms that require prolonged culturing such as *M.tuberculosis*, or those requiring totally different culture media, such as cell lines for viruses, or *Mycoplasma spp* would equally be missed[67].

Medical staff working in the ICU, pointed out that water shortage in the Unit is a chronic problem and this has had a direct impact on their regularity of hand washing practice. The lack of adherence to scrubbing protocol was related to the appearance of bruises and the attended risks, despite the importance attached to it in preventing transmission of infection[61,62].

Handwashing is the cornerstone of infection control between patients, healthcare providers, and other patients. Lack of compliance and improper technique increase the risk of infections. A simple handwashing habit is expected to eliminate many of these infections, decreasing the cost of healthcare and reducing hospital morbidity and mortality. The lesson of Semmelweis was learned long ago; yet despite consistent reminders in the literature, it appears to have been largely forgotten by healthcare providers[22].

Borgatta et al, also noted the clear advantages of appropriate hand-washing and glove use, in reducing the spread of infectious organisms from patient to staff, from patient to patient, and from staff to patient[68]. However, this practice too, can have adverse effects, excessive hand-washing, mechanical irritation from scrubbing, use of germicides, and wearing of gloves can result in

irritant and allergic dermatitis, which will lead to an increased risk of infection to both the worker and the patient. While these are or could be problems, that hinder regular hand-washing in our ICU, in many studies conducted world wide, it has been shown that most endemic nosocomial infections are transmitted by the hands[62] and we stand to loose much if for any reason, hand-washing will not be seriously encouraged in the ICU. Newson and Rowland observed that, single soap wash completely removed all bacteria from the glove, and was more than a thousand times more effective on the glove than on the hand[69]

Urinary tract infections, afflicted 94% of the patients who were admitted to the ICU during the study period. (The presence of this infection did not prevent these patients from suffering from other nosocomial infections at the same time). UTI resulted from prolonged use of indwelling urinary catheters. Our result compare well with study by Warren where they found that bacteriuria was the most common infection acquired in long term care facilities, and was usually associated with catheterisation[70].

Bologna et al found that indwelling urinary catheters are the leading source of nosocomial urinary tract infections, and the commonest

bacterial isolates were *Escherichia coli, Klebsiella spp, Proteus spp,* and *Pseudomonas aeruginosa*[70,71]. Seriously ill patients in the ICU, are usually too sick or unconscious to ask for urine bottles or bedpans, whenever they want to micturate, so they are usually catheterised despite the risk. Several studies have been carried out elsewhere to try and see if this problem could be contained or eliminated altogether and there are promising results with the use of hydrogel/silver -coated catheter[71,72]. However, promising as these results may be, the cost and availability of such catheters in our environment limits their use[71,72].

Bacteraemia accounted for about 10% of the infections acquired in the ICU. Intensive Care Unit patients show a higher risk of developing a bloodstream infection than in ordinary ward patients[73]. The urinary tract is the main source of hospital acquired secondary bloodstream infections. Nosocomial urinary tract infection is promoted by bladder catheterization in the vast majority of cases. Aerobic gram negative bacilli are the most prevalent agents of bloodstream infection secondary to nosocomial urinary tract infections[73]. In our study, aerobic gram negative bacilli accounted for about 40% of all the isolates.

In other studies, it has been shown that the increased use of intravenous catheters, contribute to an increase in bacteraemic episodes, as these catheters form the foci for bacteraemic infection[74]. This did not have any contribution in this study, as these catheters were not routinely employed in ICU patient care.

In another study, Topi found that, low respiratory tract presents the most frequent localization of ICU infections[53], also Jang et al, found that the most frequent source of blood stream infection was the lower respiratory tract, which accounted for 32.6%. It was then suggested that, the prevention of lower respiratory tract bacteria colonization and nosocomial pneumonia are crucial for reducing the incidence of nosocomial gram negative bacteremia in the ICU[53,75]. Therefore from this observation it would be possible to explain the isolation of *S.aureus* in the blood samples as those patients could have been suffering from pneumonia caused by this organism.

S.epidermidis was isolated in some cases, this could have resulted from contamination of the specimen with normal flora of the skin, though in neutropenic patients, for example, those who have undergone bone marrow or solid organ(Kidney, Heart, Liver, Pancreas et cetera) transplants. *S.epidemidis* is an important organism causing bacteraemia, as reported by Young, who found that the incidence of *S.epidermidis* had outnumbered the combined total of

P.aeruginosa, and *K.pneumoniae* bacteremias[76].

About 45% of samples did not yield any growth despite a very high index of suspicion in the patients, the reason could have been the absence of culture media to isolate other organisms like anaerobes, fungi or viruse as reported others[77,78,79].

Fourrier et al, established, in a study done on ICU patients, that the amount of dental plaque increased during ICU stay and colonization of the dental plaque was either present on admission or acquired in patients admitted there[80]. In the same study, he also showed that positive dental plaque culture was significantly associated with subsequent nosocomial infections including bacteraemia. This presents us with, a potential area for future research on another important source of certain infectious organisms that could inflict nosocomial infections on our patients.

Surgical wound infections afflicted 16.5% of the patients in this study, and the main organisms that were isolated as being responsible for their infection were gram negative bacteria 81.93%, while *S.aureus* 9% was the only micro-organism of the gram positive bacteria that was isolated. Hauer et al, found that postoperative

wound infections constituted 15.6% of the hospital acquired infections[81]. Rangel-Frausto et al, in another study done in Mexico, found that deep surgical site wound infection accounted for 9.3% of the nosocomial infections, he also found that gram negative organisms accounted for 36.6%, while *S.aureus* accounted for 11.1% of the same[81].

Shija, in 1973 while looking at the incidence and pattern of sepsis among general surgical in-patients at Muhimbili hospital, found the most common isolates were *Proteus spp, Klebsiella spp* and *S.pyogenes*[83]. The pattern of micro-organisms does not seem to have changed much over the past 27 years except with the isolation of *P.aeruginosa,* which in this study accounted for 36.4% as compared to 6% isolated then[83]. The absence of coliforms among the organisms which were isolated in our study, is rather surprising, as one would have thought that, those organisms which were isolated from the beddings would have contaminated and infected the surgical wounds more easily.

Methicillin resistant *S.aureus* is one of the most important micro-organisms in nosocomial infections. The hospital staff working in the MRSA endemic wards are known to have MRSA in the nasal cavity[84].

Masano et al, in one study, attained an isolation rate of *S.aureus* from the nasal cavity of 30% for the medical personnel working in the ICU[85]. In our study nasal isolation of *S.aureus* from the medical personnel was a constant finding, though this can not be compared to any of the findings elsewhere as the organism was not tested for methicillin resistance. This poses a challenge to us and more research needs to be done in this area, as in some studies it has been shown that strains with the same pattern of resistance that were isolated among medical staff and in the environment were also responsible for nosocomial infections[86]. This would be of necessity as proven intervention measures to reduce the carrier rate of these organisms are known and can be utilized, including application of Povidone iodine to the nares, or applying Mupirocin to the anterior nares 4-times daily for 2 days, can eliminate nasal carriage of *S.aureus*, including epidemic MRSA[87].

Together with *S.aureus* other micro-organisms were also isolated, from the nares, these were mostly gram negative rods such as *Klebsiella spp, P.aeruginosa, and Unidentified coliforms.* It is possible that these were obtained from the ICU environment, as most patients had these organisms, or the staff could have contaminated themselves with these organisms while working and in turn contaminate the patients under their care, or even could have

acquired them from the community.

The axilla yielded *S.aureus, S.epidermidis and Klebsiella spp.* In the absence of strain typing it would be difficult to state which came first whether the organisms on the medical staff and the environment or the organisms found in patients to establish a firm causal association role of nosocomial infection in the ICU. But as can be seen, there is a statistical significance in the possibility that the organisms which were found in patients had their origin in staff members except for *Pseudomonas aeruginosa.* But conclusive evidence could only be arrived at if strain typing was done to the isolates from the medical staff and those obtained from the patients.

Hair was not utilized in studying the micro organism carrier role in both patients and the medical staff working in the ICU, this was indeed a missed opportunity, as there are studies that have confirmed overwhelmingly the presence of pathogenic bacteria in the hair[88]. It would serve a good purpose in future studies to include hair among specimen from the medical workers and patients in studies of this kind, as no head gears are worn at any time in the unit.

Resistance to antimicrobial agents is an evolving process, driven by the selective pressure of heavy antibiotic use in individuals living in close proximity to others. Flaherty and Weinstein, have shown that, the intensive care unit, crowded with debilitated patients who are receiving broad spectrum antibiotics and being cared for by busy physicians, nurses, and technicians, serves as an ideal environment for emergence of antibiotic resistance[89].

In our study we established the antimicrobial susceptibility pattern for all the micro-organisms we isolated. It was found that *S.aureus* isolates were sensitive to methicillin (>90%) while only moderately sensitive to Erythromycin and Tetracycline (around 60%), but resistant to Penicillin G (as only 8% were sensitive). This could not be compared to any study done elsewhere as prevention and control strategies have focused on MRSA, Vancomycin-resistant Enterococcus, and extended-spectrum beta-lactamase-producing Gram-negative bacilli among others[89,90]. These are currently not routinely being done in the laboratory at the Centre, though it would be interesting to get a general susceptibility profile of these micro-organisms.

The gram-negative organisms isolated were *E.coli, Proteus spp, Klebsiella spp, Pseudomonas aeruginosa* and Unidentified coliforms,

These organisms were generally sensitive to gentamicin. These findings are similar to that of Edgeworth et al, who found that gentamicin resistance among gram-negative organisms had not increased during a 25-year period, despite being one of the most frequently prescribed antibiotic in the ICU[91]. Cristino found that the use of antibiotics for prophylaxis and in therapy is associated with the development of resistance in the hospital and in the community[92]. Since gentamycin is rarely used in that context for prophylaxis in the ICU, this might explain why resistance is not a major problem with it.

Klebsiella spp was the only organism that was found sensitive to augmentin and to a certain extent tetracycline, while other micro-organisms were overtly resistant. *E.coli* was the only one sensitive to chloramphenicol. These organisms were generally resistant to Ampicillin. This could be explained by the common prescription habit to which this antibiotic has been exposed to in our set up[93]. Weber et al, found that, patients infected with resistant strains of bacteria are more likely to have received prior antimicrobials, and hospital areas that have the highest prevalence of resistance, also have the highest rate of antibiotic use[90]. There is no better place in the hospital that fulfills such conditions than the ICU.

Most *P.aeruginosa* isolates were sensitive to gentamicin and

ceftriaxone. Sensitivity to kanamycin and colistin was not routinely conducted due to their unavailability.

In our environment the second line drugs for gram negative micro-organisms are ceftriaxone, ceftazidime and ciprofloxacin. Sensitivity tests results show ceftriaxone to be generally active against all gram negative microbes, the sensitivity to ceftazidime and ciprofloxacin cannot be commented upon as tests conducted were not inclusive of all the organisms all the time. Basing our confidence in these findings, where 100% of Proteus, 78.7% of E.coli, 97.3% of P.aeruginosa, 93.5% of Klebsiella spp, were found to be sensitive ceftriaxone gives hope at least for now to be an antibiotic of choice against most gram negative infections in our environment. However, this poses a challenge for future comparison studies with other drugs to be carried, along similar lines in our environment, so that a range of antimicrobials will be available for choice in case of need.

Bergogne-Berezin E, noted that nosocomial infections are among the most difficult problems confronting clinicians who deal with severely ill patients. The incidence of these hospital-acquired infections varies with the size of hospitals, with specialities wards, and with many other factors such as length of stay, local trends in antibiotic usage, nursing and hygiene conditions, hospital design and geographical

distribution of patients at risk[94]. This then means, the choice of empiric antibiotic therapy, for the treatment of any nosocomial infection before susceptibility results are available, becomes very difficult, because even in those studies, no drug was found to be sensitive 100% against those organisms. This requires that each unit sets up:

1. Regular surveillance data of predominant organisms in the units at risk,
2. The surveillance of the current resistance patterns of these organisms,
3. Where there is documented infection, identification of outbreaks involving the prevalent organisms, using modern molecular techniques for typing the strain and assess cross-contamination.

Monotherapy versus combination therapy, in the treatment of those serious gram negative hospital infections was looked into, however, the choice would depend on the site of infection, the nature of the organism involved and its pattern of resistance, also the kind of antibiotic which may more or less quickly select resistant mutants[94]. Since therapy concepts vary from country to country, it is imperative that frequent collaborative studies and increasing communication between experts of different countries, make guidelines and

consensus conferences where possible to improve the management of nosocomial infections[94].

Emmerson found that, patients in the ICU are at risk of acquiring multiply antibiotic resistant gram negative bacilli as they are temporarily immunocompromised, the majority of these are of endogenous nature and necessitate the empirical use of antibiotics[95]. The misuse of antibiotics however, often leads to the selection of multi-drug resistant gram negative bacilli. Therefore, antibiotic usage in ICUs and hospital in general should be strictly controlled and used appropriately, preferably after appropriate microbiological specimens have been collected[94,96].

File TM Jr, correctly observed that, the tremendous therapeutic advantage afforded by antibiotics is being threatened by the emergence of increasingly resistant strains of microbes. Selective antibiotic pressure favouring resistant strains arises from misuse and overuse of antimicrobials, increased numbers of immunocompromised hosts, lapses in infection control, increased use of invasive procedures and devices, and the widespread use of antibiotics in agriculture and animal husbandry[97].

MRSA is a significant problem in the hospital, as are vancomycin-

resistant Enterococcus, oxacillin-resistant *S.aureus,* and multidrug resistant Gram–negative bacilli. Owing to the high rate of antibiotic use and other risk factors, a person is more likely to acquire antibiotic-resistant infection in the ICU than anywhere else, either inside or outside the hospital[97].

Responsible antibiotic use and stringent infection-control policies are needed to discourage the development of resistant strains in our fight against nosocomial infections. Strategies at containing the resistance could include:

- Rotational of antibiotics used for empiric therapy and[89]
- Use of combination of drugs from different classes.
- Restricting the use of 3rd and 4th generation cephalosporins as empiric therapy,
- Continuous monitoring and review of antibiotic policy in the hospital.

Patients admitted to the ICU with compromised respiratory function are usually put on several modes of respiratory support, mainly oxygen supplied via nasal prongs and oxygen masks or invasive positive pressure ventilation after they have been intubated. Our findings of a general prevalence of 62.5% {33% with non-invasive,

67% on invasive mode}, are consistent, with those of studies done in other centres where the incidence of nosocomial pneumonia was less frequent in the non-invasive group, that is less than 50%, as compared to the invasive group more than 80%. This could be explained from the fact that our equipment, for example clean endotracheal tubes, ventilator tubings and suction catheters harboured some pathogenic micro-organisms to begin with, some of these could have infected our patients. This is consistent with results of studies conducted in other centres which have showed similar findings. Weber et al, found that manual ventilation bags could serve as source for colonizing the respiratory tract of intubated patients and/or the hands of medical personnel[98]. Koss et al, found that contaminated respiratory therapy equipment may be responsible for the spread of pathogens to hospital patients[99].

Fagon et al, found that, patients treated with mechanical ventilation have the highest risk for developing nosocomial pneumonia and that Gram-negative bacilli are the predominant organisms responsible for pneumonia in this setting[100], though of late *S.aureus* emerged as a significant isolate. Guerin et al, provides evidence for a significantly lower incidence of ventilator associated pneumonia(VAP) associated with non positive pressure ventilation(NPPV) compared to tracheal intubation[101]. Rello et al, found that nosocomial pneumonia is a

frequent complication of mechanical ventilation in the medical–surgical ICU[102]. Ventilator-associated pneumonia does not appear to increase fatality in critically ill patients with a high mortality rate, though it significantly prolongs the length of stay in the ICU for survivors.

Promising preventive modalities for nosocomial VAP include use of a semirecumbent position, endotracheal tubes that allow continuous aspiration of secretions, and heat and moisture exchangers[103].

Surveillance of nosocomial infections in the ICU is a proven way of controlling their occurrence and minimising the consequences suffered by patients[89,90,94,104,105].

Hayanga et al, recognised the problem of MRSA among both in and out patients at the Nairobi Hospital[105]. The infection control committee through the microbiology section of the laboratory, accelerated the surveillance program which included culturing all wards, beddings, sinks, utensils, furniture and staff. The source was identified and disinfectant methods were modified to eradicate the infection, after the relentless fight against the micro-organism through the recommended methods resulted in no more cases at the

end of the year.

Hospitals must have viable infection control programmes. The prevalence of nosocomial infection in our ICU was determined at different intervals as per research protocol.

When specimens were collected from the ICU environment on a daily basis the incidence of various infections were determined and that was compared with a weekly collection of samples for a duration of one month, this was then compared with the once a month collection interval. There was no significant difference in the occurence of nosocomial infections, when the surveillance was done daily for one month or weekly for one month, [p value was 0.69 for respiratory infections, and 0.42 for urinary tract infections]. However, there was a significant difference when the interval was increased to one month, p value being less than 0.001 and 0.001 for respiratory tract infections and urinary tract infections respectively.

Therefore, if the ICU environmental trend remains the same, the most feasible interval for routine swabbing of the ICU equipment, furniture and staff for surveillance purposes is one week. Our study has shown a lower incidence of nosocomial infections in our patients, respiratory infections 10/32(31.3%), urinary tract infections

16/32(50%), and other diseases 6/32(18.7%) when the interval is one week as opposed to a once a month interval where the incidence of nosocomial infections increased in our patients, respiratory 62/105(59%), urinary tract 90/105(86%) and other diseases 20/105(19%).

It is believed that this could change if the material conditions are modified, such as introduction of disposable equipment, enforcing regular hand washing, and the use of gloves between patients contacts. Others are, placement of labels in all conspicuous areas to the ICU workers on the need to wear gloves and wash their hands, **(examples are included in the appendix)** also labels or posters on entry to the unit alerting visitors to the ICU on removing their shoes while visiting their sick relatives.

Education should be provided to medical staff on the risk factors for the development of nosocomial infections as is the case in other centres[106]. Physicians working in the ICU can contribute greatly to infection-control efforts, by acting as role models for other personnel, by paying careful attention to handwashing recommendations and barrier precautions during contact with patients and observing posted precautions[107]. They can also give feedback to other health care providers who do not adhere to handwashing recommendations

and other precautions.

The placement of invasive devices should be based on clinical need not just on convenience, and the removal of invasive devices has to be prompt when they are no longer needed clinically. Also, physicians need to exercise care in deciding initial empirical antibiotic selection, and narrow the spectrum of antibiotic therapy once a pathogen has been recovered. During ward rounds, there is a need to alert nursing staff to lapses in asepsis (for example, soiled dressing sites of intravascular catheters) and to infection-predisposing situations (e.g., aspiration-prone position of patients).

The most feared complication of nosocomial infections is death, Bueno-Cavanillas et al, found that mortality risk was 2.48 times higher in patients with a nosocomial infection than in noninfected patients[108]. This risk was higher in those patients with respiratory diseases, and in those with longer ICU stays. In their study they concluded that nosocomial infection increases the risk of death. And Weber et al, found that infection remains a significant cause of morbidity and death for patients with burns[104].

In our study, patients with bacteraemia who died accounted for 68%

of the total, this was followed by those who had respiratory tract infection (64%), UTI and surgical wound infection each accounted for about 35%. Urosepsis carries with it a very high mortality rate. In one study it was quoted to be in the range of between 25% and 60%[109]. These figures did not consider the diagnosis on admission or the occurrence of other infections in the same person.

Since post-mortem examinations were not routinely carried out in the patients who had died, this analysis is not adequate to determine the actual cause of death[117]. It was realised that the data from death certificates in cases of known nosocomial infections were not sufficient to determine whether it was the nosocomial infection that caused death or not, which calls for a an in-depth study to establish the causes of death in our patients[111]. Although a direct relationship between nosocomial infection and mortality in intensive care unit patients has not always been demonstrated formally, it is possible to conclude that nosocomial infections increase the risk of death in critically ill patients. A more precise analysis indicates that[110]:

1) This effect is highly probable for pneumonia, doubtful for bacteremia, and uncertain for urinary tract infection;
2) risk increases with duration of stay in the ICU;
3) bacterial aetiology modifies the risk; and
4) this effect is stronger in less severely ill patients, probably

because the severity of underlying disease remains the most significant factor.

Conclusion

The results of this study have shown that nosocomial infections are significantly prevalent in patients admitted to the Intensive care Unit at Muhimbili Medical Centre.

The pattern of nosocomial infections among our patients is not different from what is being reported in other centres world wide and the infections to urinary tract tops the list, followed by pneumonia, bacteraemia and surgical wounds infections, gram negative organisms are the leading pathogens in these conditions.

Equipment used in the Intensive Care Unit do harbour certain infectious micro- organisms, which may play a role in causing infections in our patients. And staff members do harbour some micro-organisms which could infect patients under their care.

For this reason, we are encouraged to wash our hands before handling patients, and to wear gloves while providing any service to patients under our care.

In the absence of a working surveillance system in place, nosocomial infections will continue being a major contributing factor to the morbidity and mortality of our patients.

The following are hereby recommended:

1. Water supply system to the unit should be improved to ensure its availability all the time, wash basins should be conveniently located in the unit to facilitate hand washing.

2. Provision of food warming facilities and dining room should be seriously looked into.

3. Health education should be conducted to all medical staff serving the Intensive Care Unit and hospital in general, on the risk factors for dissemination and acquisition of nosocomial infections among patients admitted to the unit.

4. Nasal carriers of *S.aureus* should be typed for the possibility of harbouring methicillin resistant strain, and those positive should be treated, resume work after they are declared free of the organism.

5. There is a need for setting up a hospital infection control committee, which should be comprised of Nurses, Medical officers and Microbiologists.

6. Surveillance system should be put in place, with regularly scheduled sampling of the ICU environment, staff and patients, which will monitor any emergence of new pathogens. And institute measures of combating them.

7. There is a need for introduction of bacterial filters in between the patient and the ventilator during respiratory support sessions.

8. Antibiotic usage guidance in our ICU should follow microbial prevalence, susceptibility and resistance to antimicrobial agents.

9. Antimicrobial resistance should be anticipated and means at preventing this from happening should be put in place, such as rotational of antibiotics used for empiric therapy, use of combination of drugs from different classes. Restricting the use of 3rd and 4th generation cephalosporins as empiric therapy, and continuous monitoring and review of antibiotic policy in the hospital.

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